

Supplemental Amendment/Response for application 10/037, 718 Applicants MCGINNIS ET AL. 3
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In the Claims

Please amend and add the following claims according to the following listing of claims under 37 CFR 1.121.

Listing of Claims under 37 CFR 1.121:

1-5 (CANCELED)

6. (CURRENTLY AMENDED): A process for identifying one or more bi-allelic markers linked to a bi-allelic trait-causing polymorphism in a species of creatures, comprising the acts of:

a) choosing two or more bi-allelic covering markers so that a CL-F region is systematically covered by the two or more covering markers, the CL-F region being a collection of one or more points on a two-dimensional plane map, the two-dimensional plane map having the two orthogonal dimensions of chromosomal location and least common allele frequency;

b) choosing a statistical linkage test based on allelic association for each covering marker;

c) choosing a sample of individuals for each covering marker ;

d) obtaining genotype data/sample allele frequency data for each covering marker and the sample chosen for each covering marker, and obtaining phenotype status data for the trait for each individual in the sample chosen for each covering marker;

e) calculating evidence for linkage between each covering marker and the trait-causing polymorphism using the statistical linkage test based on allelic association chosen for each covering marker and the genotype data/sample allele frequency data for each covering marker and using the phenotype status data for the trait for each individual in the sample chosen for each covering marker obtained in d); and

f) identifying those covering markers as linked to the trait-causing polymorphism which show evidence for linkage based on the calculations of e).

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7. ((PREVIOUSLY ADDED)): A process as in claim 6, wherein the CL-F region is for a species and a population and the population is a group of individuals as in the field of population genetics, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

8. (PREVIOUSLY ADDED): A process as in claim 7, wherein the CL-F region is a segment-subrange.

9. (PREVIOUSLY ADDED): A process as in claim 6, wherein the CL-F region is for a species and a population and the population is a group of individuals as in the field of population genetics, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of covering markers are not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage, wherein a chromosome or a chromosomal subregion of interest is completely covered by chromosomal segments, wherein the segments may or may not overlap, wherein the segments are short enough that polymorphisms within each segment are likely to be in linkage disequilibrium with each other, wherein each covering marker belongs to a subset of covering markers, wherein there is more than one marker in each subset, whereby there are two or more markers in each subset, wherein the markers in each subset have approximately the same allele frequencies, wherein the difference between the least common allele frequencies of any two markers in a subset does not exceed 0.15, wherein the markers in each subset are located within one segment and within each segment there are five subsets, or more or less than five subsets of covering markers, wherein the approximate allele frequencies of the markers in each subset are spaced approximately evenly over a subrange.

10. (CANCELED)

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11. (CURRENTLY AMENDED): A process as in claim 7, ~~claim 10~~, wherein the species is not human being.

12. (CANCELED)

13. (CANCELED):

14. (CURRENTLY AMENDED): A process as in claim 7, ~~claim 10~~, wherein the process uses thousands of bi-allelic covering markers.

15. (PREVIOUSLY ADDED): A process as in claim 6, further comprising the act of:

f) localizing the trait-causing polymorphism to the chromosomal location-least common allele frequency (CL-F) location of one or more markers that show evidence for linkage based on the calculations of act e), wherein the localizing uses a technique or techniques that detects gradients, wherein the detection technique or techniques uses a gradient along the allele frequency dimension.

16. (CURRENTLY AMENDED): One or more copies of a set of oligonucleotides, the set of oligonucleotides being complementary to a group of two or more bi-allelic covering markers of the same species, wherein the group of covering markers systematically cover a CL-F region, the CL-F region being a collection of one or more points on a two-dimensional ~~plane~~ map, the two-dimensional ~~plane~~ map having the two orthogonal dimensions of chromosomal location and least common allele frequency.

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17. (PREVIOUSLY ADDED): One or more copies of a set of oligonucleotides as in claim 16, wherein the CL-F region is for a species and a population and the population is a group of individuals as in the field of population genetics, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

18. (PREVIOUSLY ADDED): One or more copies of a set of oligonucleotides as in claim 17, wherein the CL-F region is a segment-subrange.

19. (PREVIOUSLY ADDED): One or more copies of a set of oligonucleotides as in claim 16, wherein the CL-F region is for a species and a population and the population is a group of individuals as in the field of population genetics, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of covering markers are not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage, wherein a chromosome or a chromosomal subregion of interest is completely covered by chromosomal segments, wherein the segments may or may not overlap, wherein the segments are short enough that polymorphisms within each segment are likely to be in linkage disequilibrium with each other, wherein each covering marker belongs to a subset of covering markers, wherein there is more than one marker in each subset, whereby there are two or more markers in each subset, wherein the markers in each subset have approximately the same allele frequencies, wherein the difference between the least common allele frequencies of any two markers in a subset does not exceed 0.15, wherein the markers in each subset are located within one segment and within each segment there are five subsets, or more or less than five subsets of covering markers, wherein the approximate allele frequencies of the markers in each subset are spaced approximately evenly over a subrange.

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20. (CANCELED):

21. (CURRENTLY AMENDED): One or more copies of a set of oligonucleotides as in claim 17, ~~claim 20~~, wherein the species is not human being.

22. (CANCELED)

23. (CANCELED):

24. (CURRENTLY AMENDED): One or more copies of a set of oligonucleotides as in claim 17, ~~claim 20~~, wherein ~~the process uses~~ there are thousands of bi-allelic covering markers.

25. (CANCELED)

26. (NEW): One or more copies of a set of oligonucleotides as in claim 17, wherein the oligonucleotides are PCR primers.

27. (NEW): One or more copies of a set of oligonucleotides as in claim 17, wherein y is 0.15.

28. (NEW): One or more copies of a set of oligonucleotides as in claim 17, wherein there are thousands of covering markers and the species is not human being.

29. (NEW): One or more copies of a set of oligonucleotides as in claim 28, wherein the species is a paleospecies, a species hybrid such as mules, an agamospecies, an ecosystem species or a plant species.

30. (NEW): One or more copies of a set of oligonucleotides as in claim 17, wherein the species is not human being and the density of covering markers is at least thousands per chromosome.

31. (NEW): One or more copies of a set of oligonucleotides as in claim 30, wherein the species is a paleospecies, a species hybrid such as mules, an agamospecies, an ecosystem species or a plant species.

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32. (NEW): One or more copies of a set of oligonucleotides as in claim 19, wherein the CL-F region is a segment-subrange, wherein the segment of the segment-subrange is the subregion of interest or the chromosome, whereby the CL-F region is a rectangular region defined by the chromosome or subregion of interest in the chromosomal location dimension and defined by the subrange in the allele frequency dimension, wherein each point in the CL-F region is N-covered to within $[L, y]$ by markers belonging to a single subset, L is the length of the longest segment of the segments that cover the chromosome or subregion of interest, y is 0.15 and $N \geq 2$.

33. (NEW): One or more copies of a set of oligonucleotides as in claim 32, wherein the subrange of the segment-subrange is the subrange 0 to less than 0.1.

34. (NEW): One or more copies of a set of oligonucleotides in claim 32, wherein $N > 2$.

35. (NEW): A process as in claim 9, wherein the CL-F region is a segment-subrange, wherein the segment of the segment-subrange is the subregion of interest or the chromosome, whereby the CL-F region is a rectangular region defined by the chromosome or subregion of interest in the chromosomal location dimension and defined by the subrange in the allele frequency dimension, wherein each point in the CL-F region is N-covered to within $[L, y]$ by markers belonging to a single subset, L is the length of the longest segment of the segments that cover the chromosome or subregion of interest, y is 0.15 and $N \geq 2$.

36. (NEW): A process as in claim 35, wherein the subrange of the segment-subrange is the subrange 0 to less than 0.1.

37. (NEW): A process as in claim 35, wherein no two covering markers in a single subset is a redundant pair of markers in extreme positive linkage disequilibrium that provide nearly identical information with respect to their linkage and association with a third polymorphism, and wherein the inclusion of a bi-allelic marker in the subset so that there would be a redundant pair in the subset would not increase the likelihood of detecting linkage and association of the trait-causing polymorphism.

38. (NEW): A process as in claim 35, wherein $N > 2$.

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39. (NEW): A process for obtaining genotype data/sample allele frequency data for each bi-allelic marker of a group of two or more bi-allelic covering markers in the chromosomal DNA of one or more individuals of a sample, each individual in the sample being a member of the same species, comprising:

a) determining information on the presence or absence of each allele of each bi-allelic marker of a group of two or more bi-allelic covering markers in the chromosomal DNA of one or more individuals of a sample, a CL-F region being systematically covered by the two or more bi-allelic covering markers, the CL-F region being a collection of one or more CL-F points on a two-dimensional map, the two-dimensional map having the two dimensions of chromosomal location and least common allele frequency; and

b) transforming the information of step a) into genotype data/sample allele frequency data for each marker of the group.

40. (NEW): A process as in claim 39, wherein the genotype data/sample allele frequency data is genotype data or sample allele frequency data, wherein the CL-F region is for a species and a population and the population is a group of individuals as in the field of population genetics, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

41. (NEW): A process as in claim 40, wherein there are thousands of covering markers.

42. (NEW): A process as in claim 41, wherein the species is not human being.

43. (NEW): A process as in claim 40, wherein there are thousands of covering markers or the density of covering markers is at least thousands per chromosome and wherein the species is a paleospecies, a species hybrid such as mules, an agamospecies, an ecosystem species or a plant species.

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44. (NEW): An apparatus for obtaining genotype data/sample allele frequency data for each bi-allelic marker of a group of two or more bi-allelic covering markers in the chromosomal DNA of one or more individuals of a sample, each individual being a member of a species, wherein the group of covering markers systematically cover a CL-F region, the CL-F region being a collection of one or more CL-F points, wherein the apparatus is a high-density array of oligonucleotides, a nylon membrane with sequence-specific oligonucleotides bound to the membrane, or is oligonucleotides bound to a glass slide or a silicon chip, wherein one or more copies of a set of oligonucleotides that is complementary to the group of two or more bi-allelic covering markers is used by the apparatus to determine the data, wherein the oligonucleotides in each complementary set are attached to the apparatus.

45. (NEW): An apparatus as in claim 44, wherein the genotype data/sample allele frequency data is genotype data or sample allele frequency data, wherein the CL-F region is for a species and a population and the population is a group of individuals as in the field of population genetics, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

46. (NEW): An apparatus as in claim 45, wherein the apparatus is a high-density array of oligonucleotides.

47. (NEW): An apparatus as in claim 46, wherein there are thousands of covering markers.

48. (NEW): An apparatus as in claim 47, wherein the species is not human being.

49. (NEW): An apparatus as in claim 45, wherein the species is not human being and there are thousands of covering markers.

50. (NEW): An apparatus as in claim 45, wherein the species is not human being and the density of covering markers is at least thousands per chromosome.

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51. (NEW): An apparatus as in claim 45, wherein there are thousands of covering markers or the density of covering markers is at least thousands per chromosome and wherein the species is not human being and the species is a paleospecies, a species hybrid such as mules, an agamospecies, an ecosystem species or a plant species.